REQUEST FOR ACCESS OF ABANDONED APPLICATION UNDER 37 CFR 1.14(a)

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In re Application of	
CARY L. QUEEN	
Application Number	**Filed**
07/310,252	2/13/1989
Group Art Unit	**Examiner**
186	Feisel

Paper No. 25

Assistant Commissioner for Patents
Washington, DC 20231

I hereby request access under 37 CFR 1.14(a)(3)(iv) to the application file record of the above-identified ABANDONED application, which is: (CHECK ONE)

L (A) referred to in United States Patent Number 5,530,101, column 1,

___ (B) referred to in an application that is open to public inspection as set forth in 37 CFR 1.11, i.e., Application No. _____, filed _____, on page _____ of paper number _____,

___ (C) an application that claims the benefit of the filing date of an application that is open to public inspection, i.e., Application No. _____, filed _____, or

___ (D) an application in which the applicant has filed an authorization to lay open the complete application to the public.

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Unit: _____

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United States Patent [19]

Queen et al.

[11] Patent Number: 5,530,101

[45] Date of Patent: Jun. 25, 1996

[54] **HUMANIZED IMMUNOGLOBULINS**

[75] Inventors: **Cary L. Queen**, Los Altos; **Harold E. Selick**, Belmont, both of Calif.

[73] Assignee: **Protein Design Labs, Inc.**, Mountain View, Calif.

[21] Appl. No.: **634,278**

[22] Filed: **Dec. 19, 1990**

Related U.S. Application Data

[63] Continuation-in-part of Ser. No. 590,274, Sep. 28, 1990, abandoned, and a continuation-in-part of Ser. No. 310,252, Feb. 13, 1989, abandoned, which is a continuation-in-part of Ser. No. 290,975, Dec. 28, 1988, abandoned.

[51] **Int. Cl.**[6] **A61K 39/395**; C07K 16/28

[52] **U.S. Cl.** **530/387.3**; 530/387.1; 530/388.22; 424/133.1; 424/143.1

[58] **Field of Search** 424/85.8, 133.1, 424/143.1; 530/387, 388.22, 387.1, 387.3

[56] **References Cited**

U.S. PATENT DOCUMENTS

4,816,397	3/1989	Boss et al.	435/68
4,816,567	3/1989	Cabilly et al.	530/387
4,867,973	9/1989	Geers et al. .	
5,225,539	7/1993	Winter .	

FOREIGN PATENT DOCUMENTS

0171496	2/1986	European Pat. Off. .
0173494	3/1986	European Pat. Off. .
0184187	6/1986	European Pat. Off. .
0239400	9/1987	European Pat. Off. .
0266663	6/1988	European Pat. Off. .
2188941	10/1987	United Kingdom .
WO86/05513	9/1986	WIPO .
WO87/02671	5/1987	WIPO .
WO89/01783	3/1989	WIPO .

OTHER PUBLICATIONS

Vitteta et al., "Redesigning Nature's Poisons to Create Anti-Tumor Reagents," Science 238:1098–1104 (1987).

Ellison et al., "The nucleotide sequence of a human immunoglobulin C(gamma)1 gene", *Nucleic Acids Res.* 10:4071–(1982).

Hieter et al., "Cloned Human and Mouse Kappa Immunoglobulin Constatn and J Region Genes Conserve homology in Functional Segments", *Cell* 22:197–207 (1980).

Sharon et al., "Expression of a $V_\lambda C_\kappa$ chimaeric protein in mouse myeloma cells", *Nature* 309:364–367 (1984).

Takeda et al., "Construction of chimaeric processed immunoglobulin genes containing mouse variable and human constant region sequences", *Nature* 314:452–454 (1985).

Tan et al., "A Human-Mouse Chimeric Immunoglobulin Gene with a Human Variable Region is Expressed in Mouse Myeloma Cells", *J. Immunol.* 135 3564–3567 (1985).

Morrison et al., "Chimeric human antibody molecules: Mouse antigen binding domains with human constant region domains," *Proc. Natl. Acad. Sci.* 81:6851–6859 (1984).

Neuberger et al., "A hapten-specific chimeric IgE antibody with human physiological effector function," *Nature* 314:268–270 (1985).

Morrison, S. L., "Transfectomas Provide Novel Chimeric Antibodies," *Science* 229:1202–1207 (1985).

Sahagan et al., "A Genetically Engineered Murine/Human Chimeric Antibody Retains Specificity for Human Tumor-Associated Antigen", *J. Immunol.* 137:1066–1074 (1986).

Liu et al., "Expression of mouse::human immunoglobulin heavy-chain cDNA in lymphoid cells", *Gene* 54:33–40 (1987).

Better et al., "*Escherichia coli* Secretion of an Active Chimeric Antibody Fragment", *Science* 240:1041–1043 (1988).

Waldmann, T. A., "The Structure, Function, and Expression of Interleukin-2 Receptors on Normal and Malignant Lymphocytes," *Science* 232:727–732 (1986).

Leonard et al., "The human receptor for T-cell growth factor," *J. Biol. Chem.* 260:1872–1880 (1985).

Farrar, J., "The biochemistry, biology, and role of interleukin-2 in the induction of cytotoxic T cell and antibody-forming B cell receptors," *Immunol. Rev.* 63:129–166 (1982).

Greene et al., "Growth of Human T Lymphocytes: An Analysis of Interleukin 2 and Its Cellular receptor", in *Progress in Hematology XIV*, E. Brown ed., Grune and Statton, New York (1986) pp. 283–301.

Verhoyen et al., "Reshaping Human Antibodies: Grafting an Antilysozyme Activity", *Science* 239:1534–1536 (1988).

Jones et al., "Replacing the complementarity-determining regions in a human antibody with those from a mouse", *Nature* 321:522–525 (1986).

Hale et al., "Remission Induction in Non-Hodgkin Lymphoma with Reshaped Human Monoclonal Antibody CAMPATH-1H", *Lancet* Dec. 17, 1988, pp. 1394–1399.

Chothia, C. and A. M. Lesk, "Canonical Structures for the Hypervariable Regions of Immunoglobulins", *J. Mol. Biol.* 196:901–917 (1987).

(List continued on next page.)

Primary Examiner—Lila Feisee

Attorney, Agent, or Firm—Townsend and Townsend and Crew

[57] **ABSTRACT**

Novel methods for producing, and compositions of, humanized immunoglobulins having one or more complementarity determining regions (CDR's) and possible additional amino acids from a donor immunoglobulin and a framework region from an accepting human immunoglobulin are provided. Each humanized immunoglobulin chain will usually comprise, in addition to the CDR's, amino acids from the donor immunoglobulin framework that are, e.g., capable of interacting with the CDR's to effect binding affinity, such as one or more amino acids which are immediately adjacent to a CDR in the donor immunoglobulin or those within about 3 Å as predicted by molecular modeling. The heavy and light chains may each be designed by using any one or all of various position criteria. When combined into an intact antibody, the humanized immunoglobulins of the present invention will be substantially non-immunogenic in humans and retain substantially the same affinity as the donor immunoglobulin to the antigen, such as a protein or other compound containing an epitope.

OTHER PUBLICATIONS

Reichmann et al., "Reshaping human antibodies for therapy", *Nature* 332:323–327 (1988).

Bird et al., "Single–chain Antigen–Binding Proteins", *Science* 242:423–426 (1988).

Huston et al., "Protein engineering of antibody binding sites: Recovery of specific activity in an anti–digoxin single–chain Fv analogue produced in *Escherichia coli*", *Proc. Natl. Acad. Sci. U.S.A.* 85:5879–5883 (1988). in *Progress in Hematology XIV*, E. Brown, ed., Grune and Statton, New York (1986) p. 283.

Kirkman et al. Journal of Expt. Med. vol. 162 Jul. 1985 358.

Uchiyama et al. Journal of Immunology vol. 126 No. 4 1981, 1393.